

Amendment to the Claims:

Please amended the claims and add new claims 73-84 as shown in the listing of the claims below which replaces all prior listings of the claims.

1. to 36. (Cancelled)

37. (Previously presented) A core/shell nanoparticle oligonucleotide conjugate comprising:

(a) a core/shell nanoparticle comprising a magnetic core and a non-alloying gold shell surrounding the core, the gold shell having a predetermined shell thickness and the core/shell nanoparticle having a mean diameter ranging from 5 to 150 nm; and

(b) oligonucleotides attached to the gold shell, wherein the non-alloying gold shell is generated on a surface of the core by simultaneous addition of a solution comprising a gold salt and a solution comprising a reducing agent to a solution containing the metal-containing core.

38. (Previously presented) The core/shell nanoparticle oligonucleotide conjugate of claim 37 wherein the oligonucleotides have a sequence complementary to a portion of a sequence of a target nucleic acid.

39. (Previously presented) The core/shell nanoparticle oligonucleotide conjugate of Claim 37 wherein the oligonucleotides include a moiety comprising a functional group which can bind to a nanoparticle.

40. (Previously presented) The core/shell nanoparticle oligonucleotide conjugate of claim 37 wherein the magnetic core comprises Fe,Co, or Ni.

41. (Previously presented) The core/shell nanoparticle oligonucleotide conjugate of claim 40 wherein the predetermined shell thickness is determined by the formula:

$$V_{\text{core}} = 4/3 \times \pi \times R^3;$$

$V_{\text{core/shell}} = 4/3 \times \Pi \times (R + A)^3$ wherein A represents the desired shell thickness and R represents the core radius;

$V_{\text{shell}} = V_{\text{core/shell}} - V_{\text{core}}$; and

$N_{\text{shell}} = d_{\text{shell}} \times V_{\text{shell}} / \text{FW}_{\text{shell}}$ wherein N_{shell} represents the amount in moles of gold in the shell, d_{shell} represents 19.3 g/ml, and FW_{shell} represents 196.97 amu.

42. (Previously presented) The core/shell nanoparticle oligonucleotide conjugate of claim 37 wherein the magnetic core comprises an alloy metal comprising FePt or FeAu.

43. (Previously presented) The core/shell nanoparticle oligonucleotide conjugate of claim 37 wherein the magnetic core comprises a metal oxide.

44. (Cancelled)

45. (Previously presented) The core/shell nanoparticle oligonucleotide conjugate of claim 43 wherein the magnetic core comprises Fe_3O_4 or Co_3O_4 .

46. (Previously presented) The core/shell nanoparticle oligonucleotide conjugate of claim 37 wherein the gold shell ranges from about 0.5 to about 2 monolayers in thickness.

47. (Previously presented) The core/shell nanoparticle oligonucleotide conjugate of claim 37, wherein the simultaneous addition of a solution comprising a gold salt and a solution comprising a reducing agent to a solution containing the metal-containing core results in a reaction mixture having a gold salt concentration of about 2 μM .

48. (Previously presented) The core/shell nanoparticle oligonucleotide conjugate of claim 47 wherein the gold salt comprises HAuCl_4 , NaAuCl_4 , KAuCl_4 , or $\text{KAu}(\text{CN})_2$.

49. (Previously presented) The core/shell nanoparticle oligonucleotide conjugate of claim 48 wherein the gold salt is HAuCl_4 .

50. (Previously presented) The core/shell nanoparticle oligonucleotide conjugate of claim 47 wherein the reducing agent comprises NaBH_4 , ascorbic acid, NH_2OH or N_2H_4 .

51. (Previously presented) The core/shell nanoparticle oligonucleotide conjugate of claim 50 wherein the reducing agent is NaBH_4 .

52. (Previously presented) The core/shell nanoparticle oligonucleotide conjugate of Claim 37 wherein nanoparticle-oligonucleotide conjugates have the oligonucleotides present on surface of the nanoparticles at a surface density of at least 10 picomoles/ cm^2 .

53. (Previously presented) The core/shell nanoparticle oligonucleotide conjugate of Claim 52 wherein the oligonucleotides are present on surface of the nanoparticles at a surface density of at least 15 picomoles/ cm^2 .

54. (Previously presented) The core/shell nanoparticle oligonucleotide conjugate of Claim 53 wherein the oligonucleotides are present on surface of the nanoparticles at a surface density of from about 15 picomoles/ cm^2 to about 40 picomoles/ cm^2 .

55. (Previously presented) A method for making core/shell nanoparticle oligonucleotide conjugates comprising

(a) providing core/shell nanoparticles comprising magnetic cores and non-alloying gold shells surrounding the magnetic cores, the gold shells having a predetermined thickness and the core/shell nanoparticle having a mean diameter ranging from 5 to 150 nm, wherein the core/shell nanoparticles are prepared by treating the magnetic cores by simultaneous addition of a solution comprising a gold salt and a solution

comprising a reducing agent so as to form a reaction mixture having a gold salt concentration of about 2 uM; and

(b) contacting the oligonucleotides with the core/shell nanoparticles in a first aqueous solution for a period of time sufficient to allow some of the oligonucleotides to bind to the nanoparticles;

(c) adding at least one salt to the aqueous solution to create a second aqueous solution; and

(d) contacting the oligonucleotides and nanoparticles in the second aqueous solution for an additional period of time to enable additional oligonucleotides to bind to the nanoparticles.

56. (Previously presented) The method of Claim 55 wherein the oligonucleotides include a moiety comprising a functional group which can bind to a nanoparticle.

57. (Previously presented) The method of Claim 55 wherein all of the salt is added to the water in a single addition.

58. (Previously presented) The method of Claim 55 wherein the salt is added gradually over time.

59. (Previously presented) The method of Claim 55 wherein the salt is selected from the group consisting of sodium chloride, magnesium chloride, potassium chloride, ammonium chloride, sodium acetate, ammonium acetate, a combination of two or more of these salts, one of these salts in a phosphate buffer, and a combination of two or more these salts in a phosphate buffer.

60. (Previously presented) The method of Claim 59 wherein the salt is sodium chloride in a phosphate buffer.

61. (Previously presented) The method of Claim 55 wherein nanoparticle-oligonucleotide conjugates are produced which have the oligonucleotides present on surface of the nanoparticles at a surface density of at least 10 picomoles/cm².

62. (Previously presented) The method of Claim 61 wherein the oligonucleotides are present on surface of the nanoparticles at a surface density of at least 15 picomoles/cm².

63. (Previously presented) The method of Claim 62 wherein the oligonucleotides are present on surface of the nanoparticles at a surface density of from about 15 picomoles/cm² to about 40 picomoles/cm².

64. (Previously presented) The method of Claim 55 wherein the the magnetic cores comprise a metal oxide, Fe, Ni, Co, FePt or FeAu.

65. (Previously presented) The method of claim 64 wherein the gold salt comprises HAuCl₄, NaAuCl₄, KAuCl₄, or KAu(CN)₂.

66. (Previously presented) The method of claim 65 wherein the gold salt is HAuCl₄.

67. (Previously presented) The method of claim 64 wherein the reducing agent comprises NaBH₄, ascorbic acid, NH₂OH or N₂H₄.

68. (Previously presented) The method of claim 67 wherein the reducing agent is NaBH₄.

69. (Previously presented) A method of detecting nucleic acid bound to a surface comprising:

- (a) providing core/shell nanoparticle conjugates of claim 37;
- (b) providing a surface having nucleic acid bound thereto;

(c) contacting the nucleic acid bound to the surface with the core/shell nanoparticle oligonucleotide conjugates under conditions effective to allow hybridization of oligonucleotides bound to the core/shell nanoparticle oligonucleotide conjugates with the nucleic acid bound to the substrate in the presence of an external magnetic field so as to accelerate movement of the core/shell nanoparticle oligonucleotide conjugate to the surface to promote hybridization between the nanoparticle conjugate and the nucleic acid;

(d) removing from the surface any unbound nanoparticle conjugates; and

(d) observing a detectable change brought about by hybridization of the nucleic acid with the nanoparticle conjugates.

70. (Previously presented) The method of claim 69 wherein the core/shell nanoparticle oligonucleotide conjugate comprises Fe_3O_4 /gold core/shell nanoparticles.

71. (Previously presented) The method of claim 69 wherein step (c) is performed by rinsing the surface with a wash solution or reversing the magnetic field.

72. (Cancelled)

73. (Previously presented) The method of claim 69 wherein the magnetic core comprises Fe, Co, or Ni.

74. (Previously presented) The method of claim 69 wherein the magnetic core comprises an alloy metal comprising FePt or FeAu.

75. (Previously presented) The method of claim 69 wherein the magnetic core comprises a metal oxide.

76. (Cancelled)

77. (Previously presented) The core/shell nanoparticle oligonucleotide conjugate of claim 69 wherein the magnetic core comprises Fe_3O_4 or Co_3O_4 .

78. (Previously presented) The method of claim 69 wherein the gold salt comprises HAuCl_4 , NaAuCl_4 , KAuCl_4 , or $\text{KAu}(\text{CN})_2$.

79. (Previously presented) The method of claim 78 wherein the gold salt is HAuCl_4 .

80. (Previously presented) The method of claim 69 wherein the reducing agent comprises NaBH_4 , ascorbic acid, NH_2OH or N_2H_4 .

81. (Previously presented) The method of claim 80 wherein the reducing agent is NaBH_4 .

82. (Currently amended) The method of Claim 69 wherein ~~nanoparticle-oligonucleotide conjugates are produced which have~~ the oligonucleotides are present on surface of the core/shell nanoparticle oligonucleotide conjugates ~~nanoparticles~~ at a surface density of at least 10 picomoles/ cm^2 .

83. (Currently amended) The method of Claim 82 wherein the oligonucleotides are present on surface of the core/shell nanoparticle oligonucleotide conjugates ~~nanoparticles~~ at a surface density of at least 15 picomoles/ cm^2 .

84. (Currently amended) The method of Claim 83 wherein the oligonucleotides are present on surface of the core/shell nanoparticle oligonucleotide conjugates ~~nanoparticles~~ at a surface density of from about 15 picomoles/ cm^2 to about 40 picomoles/ cm^2 .

85. (Previously presented) The method of claim 69 wherein the predetermined shell thickness is determined by the formula:

$$V_{\text{core}} = \frac{4}{3} \times \pi \times R^3;$$

$V_{\text{core/shell}} = \frac{4}{3} \times \pi \times (R + A)^3$ wherein A represents the desired shell thickness and R represents the core radius;

$$V_{\text{shell}} = V_{\text{core/shell}} - V_{\text{core}}; \text{ and}$$

$N_{\text{shell}} = d_{\text{shell}} \times V_{\text{shell}} / \text{FW}_{\text{shell}}$ wherein N_{shell} represents the amount in moles of gold in the shell, d_{shell} represents 19.3 g/ml, and FW_{shell} represents 196.97 amu.